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| 09/926,218 | 01/28/2002 | Arne Holmgren | P21480 | 8453 |
| 7055 7590 12/24/2008 GREENBLUM & BERNSTEIN, P.L.C. 1950 ROLAND CLARKE PLACE RESTON, VA 20191 | | | | |
| EXAMINER KATAKAM, SUDHAKAR | | | | |
| ART UNIT 1621 | | PAPER NUMBER | | |
| NOTIFICATION DATE 12/24/2008 | | DELIVERY MODE ELECTRONIC | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gbpatent@gbpatent.com

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Office Action Summary

Application No.

09/926,218

Applicant(s)

HOLMGREN ET AL.

Examiner

Sudhakar Katakam

Art Unit

1621

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 October 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13-19 and 26-28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13-19 and 26-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/02)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Status of the application

1. Receipt of Applicant's remarks and arguments filed on 14th Oct 2008 is acknowledged. The arguments for the rejection are not found persuasive and as such, the following rejection has been maintained.
2. Claims 13-19 and 26-28 are pending in this application.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 13-19 and 26-28 are again rejected under 35 U.S.C. 102(b) as being anticipated by **Engman et al** (5/13/08 IDS document 1).

Engman et al disclose a method for reduction of a substrate with thioredoxin reductase, comprising combining the thioredoxin reductase, the substrate, selenium compound and NADPH in vitro conditions to reduce the substrate, wherein the substrate is thioredoxin and selenium compound [see Table 1, page 4601] is a competitive inhibitor for the thioredoxin [see Results]. **Engman et al** also disclose selenium in the form of selenite (selenium compound) is a substrate for the reduction by mammalian thioredoxin reductase [page 4600, 2nd paragraph]. The listed selenium compounds by **Engman et al**, specifically the following compound



| R ₁ | R ₂ |
|----------------|--|
| H | CH ₂ COPh |
| H | CH ₂ COC ₃ H ₄ -4-NO ₂ |
| H | C ₂ H ₄ -2,4-(NO ₂) ₂ |
| CONHPh | C ₃ H ₄ -2,4-(NO ₂) ₂ |
| CONHPh | SC ₈ H ₁₇ |

_____, reads on the applicants substrate.

In view of the above disclosures, viz., selenium compounds are competitive inhibitors and selenite is a substrate for thioredoxin reductase, selenium compounds inherently possess the properties of thioredoxin, and therefore, the selenium compounds expected to act as a substrate for the thioredoxin reductase.

In the reduction process, the reduced thioredoxin is useful for the conversion of hydrogen peroxide to water, which means it reduces the peroxide in the cell, with the help of thioredoxin peroxidase. More the substrate more production of reduced thioredoxin, which in turn enhances the peroxidase activity. The claims 15 and 16 have two substrates, viz., thioredoxin and selenium compound, which produces more reduced thioredoxin, which anticipates the enhancement of the peroxidase activity. Hence the claims 15-16, 18-19 and 27-28 are anticipated.

Thioredoxins are electron donors. The Km for thioredoxin is less than the selenium compound for the enzyme. The claims 17 and 18 comprises both thioredoxin and selenium compound in the enzymatic reaction. The unreacted selenium compound

expected to oxidize the reduced thioredoxin. Hence the claims 17 and 26 are anticipated.

Response to Arguments

5. Applicant's arguments filed on 14th Oct 2008 have been fully considered but they are not persuasive for the following reasons:

Applicants argue that Engman was looking at ebselen as an inhibitor, Engman used conditions wherein ebselen is used as an inhibitor and not as a substrate.

The examiner contends, however, that **Engman et al** clearly disclosed a method for reduction of a substrate with thioredoxin reductase, comprising combining the thioredoxin reductase, the substrate, selenium compound and NADPH in vitro conditions to reduce the substrate, wherein the substrate is thioredoxin and selenium compound [see Table 1, page 4601] is a **competitive inhibitor** for the thioredoxin [see Results]. **Engman et al also disclose selenium in the form of selenite (selenium compound) is a substrate for the reduction by mammalian thioredoxin reductase [page 4600, 2nd paragraph]**. Please note that a competitive inhibitor is also a substrate. Therefore, in addition to Engman disclosure [page 4600, 2nd paragraph], the selenium compound disclosed by Engman is a substrate for thioredoxin reductase.

Applicants also argue that Engman does not disclose a method of enhancing peroxidase activity of the enzyme, and a method of preventing peroxidation of a substance comprising combining thioredoxin, thioredoxin reductase and NADPH with a substrate.

Please note that in the reduction process, the reduced thioredoxin is useful for the conversion of hydrogen peroxide to water, which means it reduces the peroxide in the cell, with the help of thioredoxin peroxidase. More the substrate more production of reduced thioredoxin, which in turn enhances the peroxidase activity. The claims 15 and 16 have two substrates, viz., thioredoxin and selenium compound, which produces more reduced thioredoxin, which anticipates the enhancement of the peroxidase activity. Hence the claims 15-16, 18-19 and 27-28 are anticipated.

Applicants also argue that Engman does not disclose a method of oxidizing reduced thioredoxin by a substrate, and a method for reducing a peroxide.

Thioredoxins are electron donors. The claims 17 and 18 comprises both thioredoxin and selenium compound in the enzymatic reaction. Both are substrates for the enzyme. The Km for thioredoxin is less than the selenium compound for the enzyme. In the assay, the unreacted selenium compound expected to oxidize the reduced thioredoxin. Hence the claims 17 and 18 are anticipated.

6. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136 (a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no even, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

7. No Claim is allowed.
8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhakar Katakam whose telephone number is 571-272-9929. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Daniel Sullivan can be reached on 571-272-0779. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sudhakar Katakam/

Examiner, Art Unit 1621

/Daniel M Sullivan/

Supervisory Patent Examiner, Art Unit 1621

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